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Smallpox, Prophylaxis and Pitfalls

DONALD W. WICZER, M.D.*

Vaccination against smallpox in its present usage is one of the most effective immunization procedures in medicine. Yet, as with most procedures in medicine, when the threat of the disease diminishes so does the interest in its prevention wane. Until the reservoirs of smallpox are eradicated the threat of this scourge of man is ever present. A constant effort should be made by the medical profession to convince the population to use available facilities to be vaccinated, especially in areas where compulsory vaccination laws do not prevail. This review attempts to present the latest information on vaccination and its complications; perhaps it will help renew interest in this procedure.

HISTORICAL REVIEW OF SMALLPOX

The threat of smallpox has been ever present since ancient times. The first clear description of the disease, according to Bloomfield,[1] is often ascribed to Sydenham, but historical literature is filled with accounts of the ravages of smallpox throughout the civilized world. One of the earliest accounts of smallpox comes from China around 1122 B.C.[2] India knew smallpox then as well as now. Of the many contagious sicknesses which the Europeans brought over to the New World to plague the Indians, smallpox was by far the most deadly. Duffy[3] states that estimates of smallpox deaths alone in Spanish America during the colonial days ran into the millions and that smallpox was one of the leading causes of death in 17th and 18th Century Europe. Accounts are even available on the proposed use of smallpox infection as a weapon of war. The colonists in North America were ravaged by the disease: Father Le Jeune reported that where he was most welcome, and where he baptized the most people, was where most people died (of smallpox). In Colonial America mild types of infection among the whites often gained virulence when passed on to the Indians and then returned to the colonists in a more malignant form. Thatcher's work, "A Brief Rule to Guide the Common People of New England How to Order Themselves and Theirs in the Small Pocks or Measles," was, according to Duffy,[3] the first medical work published in America.

Little wonder that with a disease as deadly and as feared as smallpox the literature is filled with accounts of this illness, together with descriptions of the long metamorphosis from the unsuccessful to the successful modes

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of combatting the infection, as well as the usual difficulties of introduction of new methods of control to a harassed and fearful public.

In the twentieth century, smallpox continued to be a problem; Hedrich, according to Bloomfield,[1] reported there were nearly 400,000 cases of smallpox in the United States from 1921 to 1930. Even today it is estimated that there are 400,000 cases of smallpox occurring annually throughout the world,[4,5] most of these in Asia, Africa and Central America. With the continuing ever-present threat of the disease, it has been very appropriately called "The Sleeping Giant" by Gill;[6] until it is no longer endemic in large areas of the world, no country can be assured of permanent freedom from the infection.[7]

The metamorphosis of preventive measures was a long one. In China, old crusts of smallpox victims were powdered and applied to the nostrils; in India, the skin of the forehead or arm was inoculated with preserved crusts; and in Iran, these crusts were ingested in an attempt to prevent or attenuate smallpox infection.[2]

Variolation

Variolation, or inoculation, was the first solid step along the road to the prevention of smallpox. Around the year 1700, according to Stearns,[8] a letter from Joseph Lister to Martin Lister tells of the "Chinese Transfer of Smallpox." Stearns remarks:

> It appears widely assumed that knowledge of the art of inoculation for smallpox was introduced first into England whence it spread into western Europe. Actually, close examination of the source seems to show that the knowledge of the art became the property of medical practitioners almost simultaneously in England, Italy, France, the Germanies, and Scandinavia, but it also appears that the English set the example in the practice of inoculation, and only by their reported successes the Continentals were encouraged to follow suit.

During a visit to Asia and Africa in 1717, Lady Mary Wortley Montague became aware of a Greek practice of inoculating for smallpox and had her son successfully "ingrafted."[1]

The method was simple enough. Lymph or vesicular fluid from the milder cases of variola was inoculated into healthy recipients in an effort to produce an attenuated infection and convert the recipient to solid immunity (passively acquired active immunity). Indiscriminate variolation actually disseminated the infection, yet by the 1760's the widespread use of variolation or inoculation with smallpox among the settlers in America greatly reduced the smallpox hazard.[3] Jurins' efforts in census taking to establish the value of variolation revealed that there were one to two deaths for every 6 to 11 cases of smallpox which were contracted naturally, while there was only one death for every 48 to 52 inoculated with the disease

(variolation).[8] It is readily apparent that although variolation was a major step toward control of smallpox, it had many drawbacks and was far from ideal.

Vaccination

The next important breakthrough in the fight against smallpox came with the introduction of vaccination with cowpox vaccine. Cowpox is caused by a virus (vaccinia) antigenically closely related to the variola virus. The disease is endemic in Holland and England, where it was observed to cause infection in dairy hands.[7] Although probably noted but not popularized earlier, it came to the attention of Dr. Edward Jenner of Great Britain who in 1796–1798 recognized that cowpox virus immunized against smallpox.[2] Woodvale performed the first major operation of vaccinating a large number of people. To Benjamin Waterhouse goes the credit for introducing vaccination into the United States (1800–1801).[1] Smallpox vaccine using calf lymph was licensed in the United States in 1904.[9] Today it is still the most effective immunization procedure available.[10]

McClean[11] brings us up to date on the development of smallpox vaccine production in the last 30 years: 1) improved methods of destroying contaminating microorganisms, 2) methods for reducing the amount of extraneous tissue debris, 3) cultivation of the virus in the embryonated egg and in tissue culture, 4) production of stable dried vaccines, resulting particularly from the development of drying from the frozen state, and 5) improvement in methods of titrating the potency of vaccine, mostly the result of the development of pock counting on the chorio-allantois of the developing chick. The production of stable dried vaccine is an important advance, since countries in greatest need of the vaccine usually have poor storage and refrigeration facilities. In spite of considerable instability, calf lymph virus is still preferred,[12] and its use in theUnited States is so widespread that a changeover to virus grown in embryo eggs and chick embryo tissue cultures is not inevitable.[10]

DESCRIPTION OF THE INFECTION

The virus of smallpox is highly contagious. It can be transmitted by droplet infection from a patient with smallpox who sneezes or coughs, by contact with discharge from the pox or from feces or other body discharges, and even from the dried scales or crusts.[6] During the incubation period, which is said to average 12 days, the primary multiplication of the smallpox virus occurs in the lymphoid tissue of the respiratory tract. Following this, according to Kempe, Berge and England,[13] a transient viremia occurs which eventuates in the infection of all the cells of the reticuloendothelial system. Thereafter, there is further multiplication of the virus within the cells.

Hence, between 8 and 16 days after exposure, following the multiplication of the virus in the reticuloendothelial system, the secondary and much more severe viremia begins. With the onset of this secondary viremia an influenza-like illness, with high fever, muscle pain, and severe malaise is the first clinical manifestation of the disease.[6] Three to four days later a red rash appears and, as it becomes generalized, is associated with a drop in temperature. It is at this stage that smallpox is sometimes mistaken for severe measles, since the severe viremia accompanying this early erythematous rash (which sometimes becomes hemorrhagic) may result in death before the more advanced and typical lesions of the smallpox infection appear.[1] As the illness continues the skin lesions deepen and become umbilicated, then vesicular, and, finally, pustular. The rash, which originates on the forearms and face, becomes generalized. The palms and soles are not spared. After three weeks the crusts fall off but are still infectious. The above features are often masked or overshadowed by a secondary bacterial infection with accompanying general sepsis and pneumonia. The mortality rate ranges from 30 to 60 per cent, with a higher mortality in the young and the aged.

Classically, two types of smallpox are described. Variola major is the serious illness as previously described. Variola minor, or alastrim as it is sometimes called, is caused by a virus which is antigenically identical to the variola major virus.[2] According to Downie and Macdonald,[7] variola minor occurs under two circumstances: 1) if the virus is of low virulence, or 2) if the patient has increased resistance (e.g., previous variola major or vaccination). The minor form of variola remains a mild clinical illness. The course is one of the rapid development of small, superficial lesions of brief duration, and terminating in granulomas. One might think that the difference between the major and minor forms is purely artificial, depending on the immunity of the host or virulence of the strain, "yet variola minor remains a mild disease when transferred to vaccinated or unvaccinated individuals, whereas modified or mild variola major may be, and often is, a very severe illness." The incubation period (12 days) appears to be the same length in both types, but the fever is higher and the course much more severe in variola major. An outbreak of variola minor occurred in Great Britain in 1952.[6]

TREATMENT OF SMALLPOX

The treatment of smallpox is mainly supportive care and isolation. The patient should be isolated for at least three weeks from those not yet vaccinated; contacts who are not immune should be isolated for 16 days.[6] Anything containing scales or excreta from the patient, together with all

articles of linen or clothing with which he has come into contact should be burned.

The use of gamma globulin or sera from smallpox convalescents or recently vaccinated individuals has received limited testing. Field trials, using hyperimmune vaccinal gamma globulin, were carried out in Madras, India by Kempe and associates.[13] Their results seem to indicate increased protection against smallpox from this substance.

The main weapon against smallpox seems to be in the prevention of the disease. In the present day reservoirs of infection in India, Southeast Asia, Central Africa, and Central America where infected patients may be partially protected, infection may be atypical and difficult to recognize; yet in "reintroductions" mortality is 20 to 30 per cent.[7] It is understandable that methods of preventing or attenuating the disease have been sought for hundreds of years.

VACCINATION TODAY

Whom to Vaccinate

Batson and Christie[12] feel that infants 6 weeks of age and older are eligible for vaccination; vaccination is repeated before entering school and at five year intervals indefinitely. Banker,[2] in India, feels that the best time to vaccinate is at 3 months of age; he believes that delay of primary vaccination past one year of age increases the severity of local and generalized reactions. The Ministry of Health in London has advised primary vaccination against smallpox about the third or fourth month.[14] In the United States infants are commonly vaccinated at or around the sixth month of life after the triple immunization for diphtheria, pertussis and tetanus has been completed and the first two poliomyelitis injections given. Sifontes and Mirabal Font[4] suggest the vaccination of children from allergic parents at 2 months of age. According to Miller,[10] Kempe prefers vaccination in the second year of life, for although complications are more frequent, successful vaccination is more likely. In addition to infants, those persons not recently vaccinated who enter endemic areas and those exposed to smallpox should also be vaccinated (or revaccinated). Kempe and associates[13] feel that vaccination after exposure to smallpox does not yield protective antibodies in time to prevent the disease from occurring in those not previously vaccinated even though the incubation period of vaccinia is shorter than that of variola. It is, however, a sound public health measure to vaccinate if exposed to smallpox. According to McClean,[11] "Complete protection may be expected in *most* cases if vaccination takes place within 24 hours of exposure to smallpox and modification if the patient is vaccinated within

three days of contact or exposure. Beyond that interval vaccination exerts little or no influence on the infection."

How to Vaccinate

The conventional site of vaccination is in the upper left arm,[6] using skin posterior to the insertion of the deltoid muscle.[16] This is an area not too accessible to the active infant of 6 months, and is therefore not frequently contaminated by scratching or trauma. If one wishes to avoid a visible scar, the infant may be vaccinated on the thigh; however, reactions are more likely to occur in this site.[6] The multiple pressure technique with calf lymph is routinely used. The skin is prepared by swabbing with acetone or ether. This may be preceded by washing with soap and water.[16] Alcohol is not used. One should be careful to allow the cleansing substance to dry before applying the lymph, since some of the remaining cleansing liquid may inactivate the virus. One should also be careful not to cleanse the skin too vigorously lest the continuity of the skin be injured and the likelihood of the development of secondary or satellite lesions be increased.

The vaccine is then placed on the area previously cleaned, and the needle pressed through the vaccine and against the skin at a 15 degree angle, but not so vigorously as to draw blood. This is repeated 30 times, over a 5 to 10 second period.[2] In older children or in persons being revaccinated, pressing 10 times is sufficient. Punctures should be confined to an area 2 mm. in diameter. After a period of one minute the excess vaccine is removed with gauze or cotton; the remainder is allowed to dry and the sleeve is pulled down. Generally, no dressing is applied, although a light sterile gauze with adhesive tape may be used in special cases.[6] The area should be kept clean and dry until the reaction is complete.

The aforementioned technique is the most popular in this country. According to Banker,[2] it results in no pain, less infection, less reaction, smaller scars, and a larger percentage of "takes;" little special skill is required. Other less popular methods used are incision, the linear abrasion (scarification) or scratch method, the intradermal method, or the jet injection method. A "take" must always result from successful vaccinations. Even immune persons who are revaccinated develop accelerated reactions. Interpretation of an immune reaction is controversial.[16]

NORMAL RESPONSES TO VACCINATION

In the normal course of primary vaccination the inoculated vaccinia virus multiplies locally for six to eight days. During this time viremia may develop and may last until neutralizing antibodies appear at 12 to 14 days.[17] Normally a papule appears at four to five days; this then becomes a vesicle which is accompanied by slight fever. Local tenderness and slight

lymphadenopathy ensue. A crust then forms which is firm and dark; this falls off after two weeks.[6] Lewis and Johnson[18] give the following description of the normal anticipated response in the previously unvaccinated patient:

> A papule appears at the site of inoculation on the third to fourth day, and is transformed into an umbilicated vesicle on the fifth to sixth day. By the eighth day this has developed an indurated base and inflamed areola. Resolution begins after the eleventh day, and the lesion is dry by the fifteenth day although the crust may fall off one week later.

Metastatic lesions may develop during the period of viremia. As antibodies are produced the virus disappears from body fluids. This is coincident with healing of local lesions.[17]

Three types of measurable antibodies develop within 10 days after vaccination: hemagglutination inhibitory, complement fixing, and virus neutralizing antibodies. It is the third type which is most important from an immunologic point of view.[18] In studies on army recruits, Kempe and associates,[13] using neutralization tests, found the best antibody level to occur four to six weeks after vaccination. Lundström[5] found the greatest antibody level at four to eight weeks after vaccination.

Banker[2] states that a satisfactory immunity is present for three years, beginning eight days after a successful primary vaccination or from the date of revaccination. Patients with some prior immunity who are revaccinated have what is called a vaccinoid, immune or accelerated reaction. This reaches its height in from two to seven days and then fades rapidly. The so-called "immediate response" to vaccination, according to Lewis and Johnson,[18] is the development of a papule which reaches its maximum size in 24 to 48 hours. It is considered by them to be an allergic reaction and to confer no immunity.

The "no-take" reaction deserves comment. Early in life, passively acquired immunity may interfere with the dermal infection with live vaccinia virus and result in a true "no-take"[15] or perhaps an accelerated reaction.[11] The latter reaction is accompanied by a rise in antibody titer, even though no scar results. This is an example of passive-active immunization.[15] The failure to develop a skin reaction of any sort is usually, however, the result of faulty technique in virus production or storage resulting in inactive virus being used; although unlikely, it may also be due to an error in the technique of vaccination. Batson and Christie[12] suggest the following to insure a high per cent of reactors: 1) adequately preserved live virus vaccine, 2) thoroughly cleansed skin, 3) multiple pressure method, 4) removal of excess vaccine with sterile dry sponge, 5) bathing of the vaccinated area daily with soap and water, drying the skin by blotting (many would dis-

TABLE 1 (from Lewis and Johnson[18])

Cutaneous Manifestations of Human Vaccinia:

I. Local Reactions
   A. Primary vaccinia
   B. Accelerated reactions
      1. vaccinoid
      2. immediate

II. Secondary Inoculation Reactions
   A. Satellite lesions
   B. Eczema vaccinatum

III. Generalized Reactions
   A. Due to hematogenous dissemination of vaccinia virus
      1. progressive vaccinia (vaccinia gangrenosa, vaccinia necrosum)
         a) agammaglobulinemic
         b) dysgammaglobulinemic
      2. generalized vaccinia
   B. Due to hypersensitivity to vaccinal proteins
      1. roseola vaccinosa
      2. erythema multiforme
      3. urticaria

agree with this), and 6) the wearing of loose clothing only over the lesion; no dressing, shield or other applications.

COMPLICATIONS OF VACCINATION

For purposes of convenience the many possible reactions may be divided into cutaneous manifestations of human vaccinia and miscellaneous complications.

One of the best classifications of the cutaneous manifestations of human vaccinia was proposed by Lewis and Johnson (table 1).[18] To this might be added miscellaneous reactions such as: 1) vaccinations associated with other illnesses, 2) encephalomyelitis, 3) fetal vaccinia, and 4) secondary invasion of the inoculation site by bacteria.

Of the local reactions, primary vaccinia represents the expected response in a previously unvaccinated individual; the vaccinoid reaction represents the revaccination reaction (due to prior immunologic experience with the vaccinia antigen); the immediate reaction is probably an allergic response and does not confer or indicate any immunity.

Satellite Lesions

The satellite reaction is a form of secondary inoculation reaction which results from inadvertent implantation of vaccinia virus in the same or another person.[18] Common sites are about the original inoculation site and around the mouth and lips. Wherever the integrity of the skin is broken

(*e.g.*, any dermatosis), there will be a site for possible satellite lesions or secondary inoculations. No specific therapy is needed for most of these unless they are in unusually bothersome or dangerous sites; they heal concurrently with the primary vaccination site. A particularly dangerous site of secondary inoculation is the eye.[4,5,16] Vaccinal disciform keratitis may then occur and may lead to corneal perforation and permanent blindness. This serious complication should be treated with antibiotics to prevent secondary bacterial invasion and with hyperimmune vaccinal globulin.

Eczema Vaccinatum

A special type of generalized vaccinia, eczema vaccinatum, occurs following vaccinia contact in an eczematous child. This may be due to multiple secondary inoculation but most likely results at least in part from hematogenous spread. It is one of the commonest of the more severe vaccination reactions since eczema is a common childhood dermatosis, particularly in the age group usually vaccinated. According to Johnson and Dees,[19] Martin, in 1882, coined the term eczema vaccinatum. The average time of onset of these secondary lesions is 12 days after contact with the vaccinia virus; Sifontes and Mirabal Font[4] set the time of onset at 8 to 10 days. Many of the lesions appear over the eczematous skin, but some appear over normal skin, presumably by hematogenous spreading.[5] Fresh lesions may appear until death. The patients are severely ill, and disfiguring scars may result. The mortality rate is from 4 to 40 per cent;[4] in infants the mortality rate is 40 per cent.[5] When 5,000,000 persons were vaccinated in New York City in 1947 during a one month period, generalized vaccinia developed in 45. Thirty-eight of these had pre-existing dermatitis, 28 of whom were not vaccinated but were infected from another contact who was.[10,19]

Progressive Vaccinia

The primary vaccination site, due either to an absence of gamma globulin, (agammaglobulinemic variety) or to immunologically inferior gamma globulin, (dysgammaglobulinemic variety), rather than healing with the expected response, may continue to progress slowly, enlarging and involving subcutaneous tissue, muscle and bone (vaccinia osteomyelitis) as well as skin. The reaction may progress over a period of weeks or months with metastatic processes appearing in the skin, mucosa and internal organs,[5] and finally terminating fatally usually after three to five months of illness.[4] This condition is due to a severe disturbance in immunologic response. According to Lundström,[5] Acland and Fisher described the first case in 1893. It is fortunate that this complication is rare, since all reported cases except one have terminated fatally. Carson and Donnell[17] define the features of the condition as follows: 1) prolonged course of the

illness; 2) occurrence of new lesions which enlarge, ulcerate, and do not heal; 3) demonstrable failure of antibody formation against vaccinia virus and other antigens; and 4) a high mortality rate. It is puzzling that many children with agammaglobulinemia have been vaccinated successfully without this (or any other) complication. Lewis and Johnson[18] suggest that this paradox may be explained by involvement of the properdin system in this reaction.

Generalized Vaccinia

Generalized vaccinia is a complication of vaccination, in which, due to hematogenous spread of the virus, secondary lesions similar to the primary lesion develop all over the body. These are all at the same stage of development; healing is usually rapid and is complete at the same time as the primary lesion heals—there are no scars.[5] Most patients recover and the mortality rate is low.[4] The condition is more common in older children, and the illness may be prolonged for several weeks. The cause of this complication may be a slow antibody response. Those who die probably do so because of severe viremia.

Hypersensitivity Reactions

Lewis and Johnson[18] include three examples of reactions probably due to hypersensitivity to vaccinal proteins. Roseola vaccinosa, called vaccination exanthema by Lundström,[5] looks like the rash of measles or scarlatina. No treatment is necessary and the exanthema subsides at the same time as the vaccination reaction. Erythema multiforme and urticaria, as well as purpura,[4] have resulted from vaccination and are presumed due to vaccinal protein hypersensitivity reactions.

Miscellaneous Reactions

It should be realized that since vaccination is so widely practiced, acute and chronic conditions existing in the patient may be exacerbated by vaccination and may in turn complicate the vaccination. Lundström[5] reports a case of an epileptic who, after vaccination, died in status epilepticus, and feels that the existence of central nervous system conditions is a contraindication to vaccination. He also reports death after vaccination in a child who had extrapyramidal symptoms, the death of a child vaccinated while he had acute appendicitis and a case of purpura and death. Sifontes and Mirabal Font[4] report severe febrile reactions with convulsions, and describe delayed healing of the primary and multiple sites of vaccination in diabetics and in patients taking steroids.

Vaccinia encephalitis or encephalomyelitis is a rare complication of vaccination occurring 10 to 13 days after vaccination and is characterized

by fever, vomiting, convulsions, and meningeal signs.[10] If the patient survives, recovery is complete. During the mass vaccination program in New York City in 1947 (aforementioned), 45 cases of encephalitis were seen, in four of which the patients died. Lundström[5] reports that an average of 2 cases a year occurs in Sweden. Sifontes and Mirabal Font[4] say this complication occurs in less than 1 in 200,000 vaccinations. They report that it occurs less frequently in infants than in older children, and state that the onset is usually 10 to 13 days after vaccination (range 2 to 34 days). The reported mortality is 40 per cent. The vaccinia virus has not been cultured from the spinal fluid, and it is not possible to ascribe this condition to the direct action of the virus.

Fetal vaccinia is a very unusual condition. Lundström[5] states that only two cases have been reported in the literature, in each of which the mother had been vaccinated during pregnancy, and both infants died. Fifty per cent of women vaccinated between the fourth and the twelfth weeks of gestation had a course deviating from normal pregnancy; abortions, stillbirths, malformed infants, and premature infants were the main conditions resulting. Kempe and Benenson[15] studied passive immunity in newborn infants and indicated that the placental tissue stores and transfers the immunity substance, so that passive active immunization is possible in the newborn infant. All authorities agree that because of the possibility of fetal vaccinia or an abnormal outcome of the pregnancy, it is best not to vaccinate in the first trimester of pregnancy. If possible, it would be even better not to vaccinate women at any time during their pregnancy, although sometimes this is unavoidable for various reasons.

Secondary invasion of the inoculation site by bacteria can occur and is, in fact, probably the most common of all complications of vaccination.[4] Hemolytic staphylococcus aureus is the most common invader.[4,17] To avoid this complication and to decrease secondary pyogenic infection, thorough cleansing of the skin before vaccinating and adequate care of the vaccination site, with avoidance of scratching, and the use of clean clothing, and general cleanliness are necessary. Antibiotics should be used as indicated in treating this complication.

Clostridium infection, particularly tetanus, has occurred, presumably gaining entry through the vaccination site. This has been associated with the use of protective shields or tightly fitting dressings[4] which allow this anaerobic organism to multiply freely.

PRECAUTIONS

Certain precautions, concerning vaccination become obvious and are worth repeating:

1) Never vaccinate a person with a skin disease.

2) Never vaccinate an intimate contact of a person with a skin disease before separating him from the individual with dermatosis.
3) Do not vaccinate a person with a gamma globulin disorder.
4) Keep the vaccination site clean at all times; avoid contamination; use clean, white, long sleeved shirts daily.
5) Avoid covering the vaccination with a dressing; if a dressing is necessary use a thin sterile cotton gauze, applied loosely.
6) Clean skin carefully (but do not injure it) prior to vaccination.
7) Do not vaccinate malnourished or anemic children.[11]
8) Do not vaccinate patients in acute febrile states.
9) Do not vaccinate pregnant women, particularly in their first trimester.
10) Vaccinate initially before the child is one year old.
11) Vaccinate infants who come from allergic families at 2 months of age.
12) Do not vaccinate the poorly controlled diabetic.
13) Do not vaccinate patients with serious illnesses, or patients taking adrenal cortical steroids.
14) Do not vaccinate patients with epilepsy or central nervous system illnesses.
15) Be familiar with how to vaccinate, when to vaccinate and the complications of vaccination and their treatment.

HYPERIMMUNE VACCINAL GAMMA GLOBULIN

Hyperimmune vaccinal gamma globulin is the mainstay of treatment of the more serious forms of vaccination complications. Kempe and associates[13] have done much of the work in preparing this globulin and employing it in treatment of vaccination complications in this country. Since the highest antibody levels occur four to six weeks after vaccination, the blood of donors, frequently military recruits, is drawn at this time and the material so obtained is fractionated. About 5 ml. of vaccinal hyperimmune-gamma-globulin-containing-protein is isolated from every 150 ml. of the whole blood drawn.[5] The immune globulin obtained by Lundström is in the form of a 12 per cent solution of Cohn's fraction II of which 95 to 98 per cent consists of gamma globulin. When vaccinia virus and the serum are inoculated into the chorio-allantoic membranes of chick embryos, a greater than 50 per cent pock count reduction over that obtained in controls is considered to be evidence of a potent vaccinal hyperimmune gamma globulin. The antivaccinal antibody content is at least three times that of ordinary gamma globulin.[13] For prophylaxis of smallpox or of any anticipated vaccination reactions the exact dose of hyperimmune vaccinal gamma globulin remains undetermined. Fox and Pica[20] state that probably 0.03 ml. per pound of body weight is the minimal effective dose. Doses of 0.06 ml.

to 0.12 ml. per pound of body weight probably give more effective protection. Material should be given as early as possible after exposure, and smallpox revaccination should follow within 12 to 24 hours. The dosage of hyperimmune gamma globulin used to protect against smallpox after contact in the Madras, India, field trials,[13] was 0.2 ml. per pound of body weight in adults, 0.05 ml. per pound of body weight in children, and 0.1 to 0.2 ml. per pound of body weight in infants under one year of age. There have been no good controlled studies of hyperimmune vaccinal globulin since the complications of vaccination have been few and it is unjustified to withhold a life-saving drug.

If hyperimmune vaccinal gamma globulin is unavailable, ordinary gamma globulin may be tried. If this is used a dose of 1 ml. per Kg. of body weight is probably necessary.[5]

According to Fox and Pica,[20] the therapeutic dosage of hyperimmune gamma globulin in the treatment of eczema vaccinatum is 0.3 ml. per pound of body weight. When the total dose exceeds 10 ml. it may be divided and given at separate injection sites to decrease the trauma of the injection. In a report by Kempe, Berge, and England[13] of 14 infants with eczema vaccinatum given 0.6 ml. per Kg. of body weight of hyperimmune gamma globulin "on one or two occasions," two deaths occurred. In both these cases the infants had received injections of the globulin late in the course of their illness. In the surviving cases no new lesions appeared after the children had received the globulin. Hyperimmune vaccinal gamma globulin is therefore of great aid in treatment here. Some patients with eczema vaccinatum may make a prompt recovery on no specific therapy; this is presumably due to a good antibody response. Kempe and associates have also shown that when vaccination is absolutely necessary in patients with eczema, it may be done without complication under the cover of hyperimmune vaccinal gamma globulin. They vaccinated eight children with eczema and also gave 0.6 ml. per Kg. of body weight of the immune globulin together with the vaccination. No complications occurred; all had primary vaccinal reactions. They also gave the same dose of globulin to six infants with eczema who were accidentally exposed to vaccinia. No complications occurred although two infants had a rise in antibody titer.

In the treatment of progressive vaccinia, Sifontes and Mirabal Font[4] suggest a dose of 0.6 ml. per Kg. of body weight of hyperimmune vaccinal gamma globulin, or 2.5 to 4.0 ml. per Kg. of body weight of pooled gamma globulin. The one reported child with progressive vaccinia who survived[21] was treated with hyperimmune vaccinal gamma globulin after involvement of large areas of skin, muscle and bone. This 4½ year old child was given five 10 ml. doses altogether over a course of six weeks.

Kempe and associates[13] have treated 8 cases of generalized vaccinia with

0.6 ml. per Kg. of body weight of hyperimmune globulin. No new lesions appeared after the injection of globulin was given, and there were no fatalities.

SUMMARY

A brief historical review of smallpox is presented. The development of vaccination, how to vaccinate, and when to vaccinate are indicated. The complications of the vaccination are discussed as well as their treatment, particularly the development and use of vaccinal hyperimmune gamma globulin. Precautions in the use of vaccination are enumerated. A plea is made for less complacency, more vigilance, and more interest in vaccination in the fight against smallpox.

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Fractures in Children: A Two Year Review of Experience at Children's Hospital

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In a four month period from August through November 1958, 1,352 accidents were treated in the Outpatient Department of Children's Hospital. Of these, 180 (13.3 per cent) were fractures. Records for the years 1957 and 1958 show that a total of 913 children were treated for 1,122 fractures at this hospital. Two hundred fifty-two patients (27.7 per cent) had to be hospitalized. Boys sustained fractures more frequently than girls (a 3 to 1 ratio); twice as many Negro as white children were affected. The ages ranged from birth to 16 years but the majority of the patients were between 2 and 9 years of age. The incidence was not equally distributed over the whole year and a so-called "fracture season" was noted. More fractures, i.e., 575 (63 per cent), occurred from June through September. The highest incidence occurred in June and the lowest in December. Three children (0.33 per cent) died after admission as a result of intracranial or intrathoracic complications. Thirty additional children were "dead on arrival" at the hospital as the result of automobile accidents.

The causes and frequency of the fractures are listed in table 1. The great majority, 547 (67.3 per cent), were due to "falls," while automobile accidents were responsible for 117 (14.5 per cent). Fractures attributable to sports, crush injuries, pathological fractures, and wringer injuries accounted for most of the remainder. Only 2 per cent of the total number of fractures

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were compound, emphasizing the relative rarity of this type of fracture in children.

The affected bones and the frequency of their involvement are noted in table 2. The forearm was the most common fracture site. Three hundred eighty-four fractures (34.7 per cent) involved the forearms, 79.4 per cent of which occurred in the distal third. The radius was the most frequently fractured bone (22 per cent) in children. About 55 per cent of the radial fractures were associated with a fracture of the ulna. These fractures of the distal third of the forearm in children occur very much in the same way as the Colles' fracture in adults, i.e., by falling on the outstretched forearm. Anatomical differences prohibit the application of the term "Colles' fracture" to fractures of the forearm in the distal third in young children. The

TABLE 1
Etiology of Fractures

	No. of children	%
Falls	547	67.3
At level	341	
Stairs	45	
Chair, stool	22	
Porch	23	
Tree	19	
Monkey and jungle bar	11	
Fence	9	
Swing	9	
Sliding board	8	
Bed and crib	38	
Others	22	
Vehicle Accidents	156	19.2
Automobile	117	
Tricycle, bicycle	39	
Sports	54	6.6
Ice skating	13	
Roller skating	10	
Base ball	11	
Basket ball	5	
Foot ball	6	
Wrestling	4	
Boxing	1	
Horseback riding	4	
Wringer injuries	5	0.6
Crush injuries	44	5.4
Pathological	7	0.9
Not recorded	100	
Total	913	

TABLE 2
Bones Involved

	No.	%
Radius	249	22.2
Ulna	135	12.5
Humerus	133	11.9
Clavicle	114	10.1
Tibia	106	9.4
Skull	103	9.1
Femur	74	6.5
Hand	71	6.3
Foot	46	4.1
Fibula	32	2.7
Dislocations	28	2.4
* Miscellaneous	31	2.7
Total	1,122	

* Includes ribs, spine, nose, mandible, maxilla, scapula and pelvis.

classical Colles' fracture, as Abraham Colles described it in 1814,[1] is a fracture of the carpal extremity of the radius within 1 to 1½ inches from the joint accompanied by a fracture of the ulnar styloid with dorsal displacement. The site of fracture in the distal third of the forearm in children is usually at a higher level. If the ulna is also fractured, as is frequently the case, the fracture will be found, not through the styloid, but at about the same level as that of the radius. One explanation may be the fact that the ulna styloid is not fully developed in children. If a fracture occurs within 1 or 1½ inches of the joint as in a Colles' fracture, it would usually result in a slipped epiphysis.

Fractures involving the elbow were found in 128 cases (11 per cent). About 50 per cent of these were supracondylar in type. The clavicle as well as the tibia and femur were among the more common fracture sites. Skull fractures were not uncommon but, fortunately, only 8.7 per cent of these had depressed fragments. Half of the fractures of the femur were caused by automobile accidents, and these fractures were usually transverse in type.

DISCUSSION

Of a total number of 1,122 fractures in this series, 1,106 (98.6 per cent) were treated by conservative measures (table 3). The end results were uniformly good although the follow-up is not sufficiently long in some cases. Blount,[2-9] Neviaser[10] and many others have stressed the fact that fractures in children differ from those in adults. Since the cause and nature of child-

TABLE 3

Over-all Treatment

Conservative measures		1,106 fractures (98.6%)
Open reduction		16 fractures (1.4%)
Elbow	2	
Forearm	2	
Femur	3	
Tibia	1	
Skull	8	
Total		1,122

hood fractures are simple, treatment in most instances is not complicated, and the end results are uniformly good. A simple closed reduction and immobilization with plaster of Paris is all that is needed in the majority. The surgeon should always be aware of these facts. Complicated methods of treatment are not only unnecessary but are followed by inexcusable complications.

The basic differences of fractures occurring in childhood from those occurring in adults are in healing and growth potentiality. A child's bones are not only living but growing. In children a certain amount of local deformity will be corrected by the molding process. In addition, a small degree of shortening will be compensated for by a later growth acceleration.[11-13] Therefore, a side to side apposition with about 1 cm. of overriding is preferable to an accurate end to end apposition, particularly in fractures of the femur.[8,11,14-16] Open reduction and internal fixation are rarely necessary; the only exceptions are those children in whom closed reduction fails. This occurs in some fractures of the lateral or medial condyle, the epicondyle, or the neck or head of the radius[5,7,17] and a few very rare fractures in other joints. Unnecessary surgical intervention may result in a perfect x-ray correction but is likely not only to cause soft tissue damage but also growth arrest as a result of damage to the periosteum and epiphysis; the incidence of infection is also increased.

The epiphyses should never be resected in children since this will result in growth arrest and a permanent deformity. Louis and Thibodeau[18] have warned of deformities following resection of the radial head.

The major fragment of a fracture should neither be rotated nor grossly angulated; the resultant deformity may last permanently. More accurate reduction of an angulation deformity is required when the fracture occurs in the middle third of the bone. Less accurate reduction is permissible in a younger child when the fracture is closer to the end of the bone. Condi-

tions such as open (compound), supracondylar fractures, and dislocation of any joint, with or without a fracture, require emergency care.

METHODS OF TREATMENT MOST OFTEN USED FOR SPECIFIC FRACTURES IN CHILDREN

The treatment of choice for a given fracture in adults may vary, and depends upon the nature of the fracture and site, general condition and age of the patient, and the judgment of the surgeon. In children, however, it is worthwhile to follow a simple general outline.

Hand

Splinting in the functional position is used in most fractures except for the so-called "Three-B fractures:"[4,19] 1) Bennett's fracture of the base of the thumb through the carpo-metacarpal joint with dislocation may need continuous traction and abduction with a well molded cast; 2) boxer's finger of the neck of the metacarpal bone, most commonly occurring in the fifth finger, requires hyperflexion of the metacarpo-phalangeal joint; 3) baseball (mallet) finger[19] with rupture of the extensor tendon, and/or avulsed fracture of the dorsum of the base of the terminal phalanx, needs immobilization of the distal joint by hyperextension and flexion of the midjoint of the finger.

Clavicle

A figure-of-eight bandage is the treatment of choice. Reinforcement with plaster of Paris may be necessary in older children.

Forearm

After proper reduction a circular cast or antero-posterior splints with a soft sling provide for the child's comfort. If a long arm cast is needed, approximately 90 degree flexion of the elbow should be maintained. A cast with the forearm in pronation is necessary for fractures of the distal third; neutral position between pronation and supination for fractures of the mid-third; and full supination for fractures of the upper third. These assure an unimpaired rotation mechanism of the forearm.

Elbow

After reduction a long arm cast or well molded long posterior plaster splint with the elbow in flexion is needed. The degree of flexion depends upon the amount of swelling, which may add to circulatory embarassment. If circulatory embarassment is marked, as indicated by the strength of the radial pulse, Dunlop's type[20] of side arm traction is the treatment of choice.

Careless, violent trauma to obtain reduction, or the overlooking of weak or absent radial pulse may result in a serious complication, viz., Volkmann's contracture,[6,21] and are difficult to justify. Damage to the brachial artery indicates prompt surgical intervention. Fractures of the olecranon should be immobilized with the elbow in full extension.

Humerus

A light hanging cast is the treatment of choice for fractures of the surgical neck or shaft.

Femur

Russell traction[22] is indicated in older children for fractures of the shaft. Bryant vertical traction[4,13] should be used in younger children, and followed by a spica cast after 3 to 4 weeks.

Tibia

Fractures of the tibia may sometimes require a small Steinman pin or Kirschner wire through the heel incorporated in a long leg cast in order to maintain proper alignment.

Ankle and Foot

These are adequately managed with well molded casts with or without a walking heel.

Open (Compound) Fractures

These always require emergency care. The exposed bone should always be covered properly by means of primary closure after careful debridement of the devitalized tissues and reduction of the fragments. Antibiotics and tetanus toxoid or TAT are routinely indicated.

SUMMARY

1. A review of fractures in children seen during a two year period at Children's Hospital is presented.
2. The fact that fractures in children differ from those in adults has been stressed, the principles of treatment have been reviewed, and the methods of treatment most often used outlined.
3. Of the 1,122 fractures reviewed, 98.6 per cent were treated by conservative measures. Surgical intervention was needed in only 1.4 per cent (16 cases).

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Aldrich's Syndrome

Discussion by: ALLAN COLEMAN, M.D.* AND
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Case Report by: GRACE H. GUIN, M.D.‡

In 1954, Aldrich, Steinberg, and Campbell[1] described a 6 month old boy whose illness included draining ears, eczematoid dermatitis, and bloody diarrhea, and who had a pedigree which revealed this triad to be a sex-linked recessive condition. The following is believed to be the first case of this disease diagnosed at Children's Hospital.

CASE REPORT

This 20 month old white male child with known thrombocytopenic purpura was brought to the Emergency Room of Children's Hospital because of gross bleeding from the nose and oral cavity. The child had gasping respirations and appeared quite pale. Profuse bleeding from the mouth and nose was noted. Aspiration of the oral cavity was performed immediately and artificial respiration started. He expired a few minutes later.

He was born normally after a full term uneventful pregnancy; birth weight was 7 pounds 8 ounces. At the age of 6 days, he developed diarrhea with some streaks of blood in the stool. When he was 6 weeks old an extensive purpuric rash was noted; bloody stools were again noted at that time. A platelet count was reported as 40,000 per cu. mm., and a tentative diagnosis of allergic thrombocytopenic purpura was made. A soy bean formula was prescribed; the rash subsided but the platelets remained low. He was then given cortisone therapy and later ACTH, but bi-weekly examinations of the blood for platelets showed no increase in their number. When 5 months old, he was admitted to the hospital for a blood transfusion and received 130 ml. of packed red cells. Bilateral otitis media was noted at that time.

One month later, it was necessary to hospitalize him again for a blood transfusion; two weeks prior to this admission the platelet count was reported to be 40,000 per cu. mm. Physical examination disclosed that his development and nutrition were satisfactory for a 6 month old infant. There was a petechial rash covering the chest, back and abdomen; it was especially prominent in both popliteal regions. The spleen was palpable 1.5 cm. below the left costal margin, and the liver extended 2.0 cm. below the right costal margin. The remainder of the physical examination was not remarkable.

During this hospital admission the total bilirubin was reported as 1.24 mg. per 100 ml. (0.25 mg. per 100 ml. direct, 0.99 mg. per 100 ml. indirect). An indirect Coombs' test, a lupus erythematosus preparation, and determination of cold agglutinins were all reported to be negative. One week following admission, the hemoglobin was 7.9 Gm. per 100 ml., hematocrit 27 per cent, and red cells 2.99 million per cu. mm. Red

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cell indices were MCV 90 cubic microns, MCH 27 micromicrograms, MCHC 29 per cent. A Heinz body preparation was negative. He received 150 ml. of packed red cells and was discharged on the same day with diagnoses of 1) thrombocytopenic purpura, and 2) hemolytic anemia, etiology undetermined.

He was admitted to Children's Hospital for the third time at 8 months of age with a fever of 101°F. A diagnosis of acute respiratory tract disease was made. A diffuse chronic eczema with some petechiae was noted at that time. The white blood cell count was reported as 37,300 per cu. mm., with segmented forms accounting for 89 per cent and mature lymphocytes 11 per cent. He was discharged the following day, having been placed on broad spectrum antibiotic therapy; he was also placed on prednisone at that time. He was admitted to the hospital for the fourth time at 17 months of age for bronchopneumonia which was complicated by viral gastroenteritis. He was discharged 10 days later after being treated vigorously with chloramphenicol and penicillin.

His fifth hospitalization at 19 months of age was occasioned by dyspnea of two days' duration. Rectal temperature was 103°F. Slight cyanosis and irritability were noted. He had a "moon" face. Breathing was labored, and rhonchi and coarse rales were heard throughout the lung fields. The liver and spleen were palpable. X-ray examination showed bilateral bronchopneumonia and atelectasis of the right middle lobe. The leukocyte count was 11,200 per cu. mm., with segmented forms accounting for 76 per cent, band forms 2 per cent, eosinophiles 10 per cent, lymphocytes 4 per cent, and monocytes 8 per cent. The platelets were decreased in number. The hemoglobin was within normal limits (11.6 Gm. per 100 ml.). There were 1 to 2 leukocytes per HPF and 2 to 4 erythrocytes per HPF in the urine. Fever continued until discharge despite vigorous treatment with penicillin, chloramphenicol and gamma globulin. Four days prior to his final hospitalization he was seen by an otolaryngologist who made the diagnosis of chronic otitis media and aural polyps. He did fairly well the next few days but quickly succumbed during his final illness.

At autopsy the child was noted to have the typical cushingoid appearance of patients receiving steroid therapy. There was marked pallor, and bloody fluid issued from both nasal and aural cavities. A few petechiae were scattered over the body. The lungs were indurated and presented a nodular surface; on section they revealed multiple fairly well circumscribed areas of necrotic tissue which were believed to be abscesses.

The liver weighed 20 Gm. more than normal for the age and was smooth; on section it did not appear remarkable. The spleen was smaller than is usually observed for this age group. There were three ulcerated areas in the esophagus which extended into the muscularis. The stomach and intestines contained bloody fluid. The kidneys were not remarkable. The meninges were thickened. Many of the lymph nodes were enlarged, and measured up to 2.0 cm. in diameter.

Microscopically the lymph nodes were infiltrated by varying numbers of reticuloendothelial cells. There was evidence of bronchopneumonia in both lungs, and in addition widening of the interalveolar spaces as a result of the presence of large mononuclear cells and ingrowth of fibrous tissue (fig. 1). Some of the alveolar spaces contained solid aggregates of acidophilic hyaline-like material. The areas interpreted as being abscesses on the gross examination proved to be nodules of benign-appearing monocytic cells, reticulum cells and small numbers of fibroblasts surrounding central areas of necrosis without evidence of acute inflammatory reaction. The liver disclosed a moderate number of inflammatory cells within the sinusoids. The spleen contained a reduced number of lymphocytes; there appeared to be an increase in the number of reticuloendothelial cells which were irregularly distributed throughout the organ

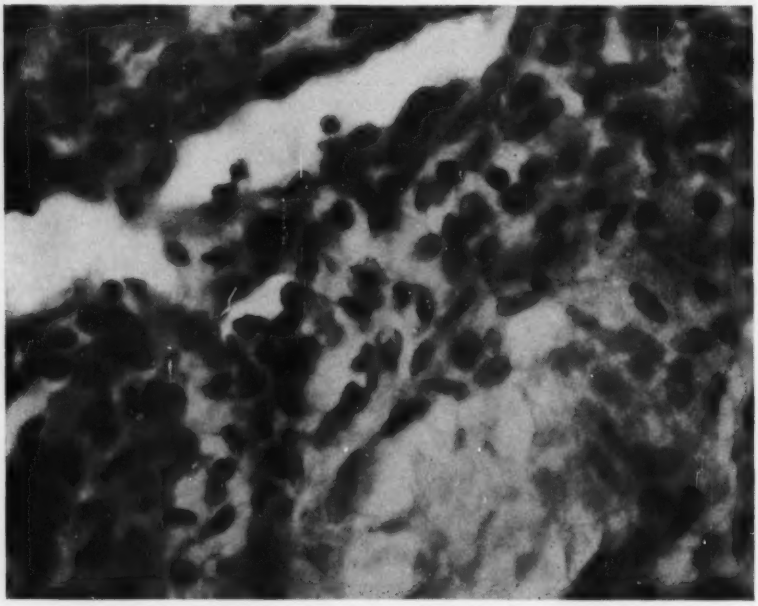

FIG. 1. Microscopic section of lung tissue showing marked thickening of alveolar wall due to infiltration of reticuloendothelial cells.

rather than confined to the germinal centers. The malpighian bodies were markedly reduced in number and indistinct in margination. The mucosa of the larynx was infiltrated by benign-appearing reticuloendothelial cells. The ulcerated areas of the esophagus revealed marked infiltration and invasion of reticuloendothelial cells similar to those appearing in the other organs; there was minimal inflammatory reaction. The bone marrow was infiltrated with similar cells; both granulocytic and erythrocytic series were depressed. The megakaryocytes appeared in normal numbers. There was marked infiltration of monocytic and reticulum cells in the pia-arachnoid. These cells extended to and invaded the adjacent cerebral cortex, and were arranged around blood vessels. Focal necrosis of the nerve tissue was evident.

Pathological diagnoses were:

1. Reticuloendotheliosis with involvement of the brain, meninges, lungs, esophagus, larynx, spleen, lymph nodes, and bone marrow.
2. Acute and chronic pneumonitis.
3. Ulceration of esophagus, with hemorrhage.
4. Cushingoid syndrome, secondary to steroid therapy.

DISCUSSION

Dr. Coleman:

There was histologic evidence that this child suffered from a type of nonlipid histiocytosis. He had classical infantile eczema in infancy which

responded satisfactorily to elimination of food allergens, a thrombocytopenic purpura which flared whenever the eczema became aggravated, and multiple pulmonary and ear infections. He always maintained an eosinophilia in the peripheral blood of 10 to 15 per cent, suggesting strongly that he had some type of underlying allergic mechanism in addition to the histiocytic proliferation.

The age of onset in this child was at two months. His initial symptom, as is described in most cases of Aldrich's syndrome, was gastrointestinal bleeding. This was followed by a purpuric rash which, as it faded, became a classical wet infantile eczema involving the cheeks, antecubital spaces and trunk. In addition he had a thick matting of the scalp, typically that of the ordinary patient with severe eczema.

Smith,[2] discussing Aldrich's syndrome, has said, "Many of the pedigrees have turned out to show that these ran through families as a sex-linked recessive." An attempt was made to trace the pedigree of this patient, but unfortunately some of the relatives pertinent to this study lived in Spain and were resentful of inquiries. It was, however, determined that two males in the proper position in the family tree died in their thirties of cerebral hemorrhage. Smith discusses the resemblance of this clinical picture to Letterer-Siwe's disease, and cites a method described by Moore[3] of examining touch preparations from the skin to obtain histiocytes and thus differentiate the two diseases.

None of the previously reported patients has survived. Huntley and Dees[4] have reported a group of five patients with this syndrome. Four of the five underwent splenectomy, but all eventually died from infections, two from meningitis and three from pneumonia.

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Dr. Leikin:

Clinically this child presented as a case of Aldrich's syndrome. The diagnosis was based on the observation of early hemorrhagic signs which were accompanied by thrombocytopenia despite the presence of normal

numbers of megakaryocytes in the bone marrow. There was a prominent atopic dermatitis. The absence of massive hepatosplenomegaly and significant generalized lymphadenopathy militated against the diagnosis of a nonlipid reticuloendotheliosis. This patient also demonstrated an eosinophilia which is usually not seen in the latter disease. The bone marrow which was studied early in the course of this patient's disease showed no increase in reticuloendothelial cells; this, however, may be a late manifestation of Letterer-Siwe's disease.

What are the various mechanisms causing thrombocytopenia? If the megakaryocytes are thought of as precursors of platelets, the first mechanism of thrombocytopenia is the absence or destruction of megakaryocytes. This can occur either by invasion of the marrow by leukemia or cancer cells, or histiocytes, or alternately by suppression of megakaryocyte production as a result of infection or administration of toxic drugs such as chloramphenicol. The second mechanism is one of inhibition of platelet production; megakaryocytes are present but platelets are not being formed. This may be due either to arrest in the maturation of megakaryocytes or an absence of the fragmentation of the cytoplasm of these cells without platelet particles being produced. The third mechanism is one of direct destruction of the platelets by a specific platelet antibody, or removal from the peripheral blood by the exchange of platelet rich blood for donor blood which may be platelet poor (seen frequently after exchange transfusions). A fourth mechanism capable of producing platelet depression is excessive destruction of platelets in the tissues. This appears to be the mechanism of the thrombocytopenia observed in the patient with thrombotic thrombocytopenic purpura.

In Aldrich's syndrome, megakaryocytes have been present in the cases reported. Occasionally they appear somewhat immature and have only a few platelets in their vicinity. However, in most reported cases, the megakaryocytes have been described as normal in appearance. In the cases studied by Krivit and Good[1] there were no platelet antibodies, and in only one case cited, again by the same authors, have any thrombotic type of lesions been seen.

It would appear, then, that the mechanism of action of the thrombocytopenia in this disease is either suppression of megakaryocyte dissolution or destruction of platelets in the blood stream. Despite the fact that no platelet antibodies have been found in the blood, the gastrointestinal tract may be highly permeable, and the allergens ingested may have a destructive action on these specific platelets. It is also possible that the platelets are more susceptible to the destructive action of allergens than those of a normal individual. Unfortunately, platelet survival studies have not been done on these patients.

Thus far the leads have not been very fruitful in determining why these

patients are so susceptible to infection. Serum levels of gamma globulin have been normal or slightly increased. Properdin levels are also normal. Studies of the motility of the leukocytes in surface phagocytosis have been within normal limits. Antibody production to specific antigens such as typhoid, mumps, pertussis, diphtheria and poliomyelitis have all showed normal response.

The only revealing study of the susceptibility of these children to infection is that of Krivit and Good[1] who found low levels of isoagglutinin titers against A and B red cells. The significance of this is uncertain, since frequently isoagglutinin titers are normally low in young infants.

The treatment of Aldrich's syndrome is that of a chronic thrombocytopenia, making use of all the available methods, and beginning with the adrenal cortical steroids. These drugs do not affect the platelet count significantly but may occasionally help vascular integrity. Platelet transfusions have been tried and are only of temporary benefit due to the short survival of even normal platelets. Platelet transfusions should be reserved for only acute severe hemorrhagic situations, since platelet antibodies are frequently and easily produced by the continued use of such transfusions.

The effect of splenectomy has been short lived in all of the cases which have been reported; the operation is of no proven value. In one report by Brubaker and Hammond,[2] however, there were 3 cases which seemed to benefit by splenectomy. The report is very brief and does not disclose the length of the follow-up period. It is possible that these patients have subsequently died of infection.

Hypoallergenic diets have not helped either the platelet deficiency or the eczematoid reactions in most of the cases reported.

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The Editor's Column

THE VIG PROGRAM

The complications of vaccination are probably more feared in urban areas of the United States than the "scourge" of smallpox itself. For that reason, physicians have watched with interest the work of Kempe, Benenson, Lundström and others with the American National Red Cross and

Armed Forces of the United States in preparing and testing vaccinia immune globulin (VIG) (See "Smallpox, Prophylaxis and Pitfalls," page 1). Recently the preparation and distribution of VIG has been announced as a regular service of the Red Cross Blood Program. However, the supply of VIG is scant; thus, physicians should be particularly careful to understand its nature and possible use.

VIG is a fraction of the blood from recently vaccinated servicemen; it contains a high titer of antibodies against vaccinia virus. The dosage which has been used in most studies of effectiveness is 0.6 ml. per Kg.

VIG has been of value in 1) preventing or lessening the severity of smallpox in persons undergoing contact, and 2) treating severe complications of vaccination such as secondary vaccination into the eye, eczema vaccinatum or generalized vaccinia and vaccinia necrosum. VIG has not been effective in treating post vaccinal encephalitis, and certainly it is not indicated in instances where vesicular lesions are not vaccinia, and in disturbing normal reactions and trivial secondary reactions.

To assure availability of consultation with physicians considering the use of VIG, a panel of volunteer Red Cross consultants has been appointed. These consultants are regionally distributed; in the near future each of the represented regions will have a supply of VIG on hand. In the District of Columbia, Maryland and Virginia area (and further covering the Middle and Lower Atlantic states) the consultants are: James H. Pert, M.D. (Associate in Medicine, George Washington University School of Medicine) Research Director, Blood Program, American National Red Cross Headquarters, Washington 6, D. C. (Republic 7-8300, ext. 543), (Residence: Chevy Chase, Maryland, Oliver 6-8375).

Alternate: Robert H. Parrott, M.D., (Clinical Professor of Pediatrics, Georgetown University School of Medicine), Children's Hospital, 2125—13th Street, N. W., Washington 9 D. C. (Dupont 7-4220, ext. 280). (Residence: Bethesda, Maryland, Oliver 2-0548).

ROBERT H. PARROTT

Book Reviews

Pathology of Infancy and Childhood. By AGNES R. MACGREGOR, M.D., F.R.C.P.E., F.R.C.O.G. 639 pp., with 388 illustrations: Edinburgh and London; E. & S. Livingstone, Ltd., 1960. The Williams & Wilkins Co., Baltimore, exclusive U. S. agents, $14.50.

Pediatric pathologists and other pathologists whose work only occasionally brings them into the field of fetal, neonatal and pediatric pathology have long expressed a desire for a book covering this area. In this volume Dr. Macgregor has covered the pathology of the fetus, the neonate, infant and child. The value of the book is enhanced by the knowledge that the author has acquired by long experience.

The section on developmental malformations is of particular value in view of the increasing importance of the developmental defects which the pediatrician, surgeon and pathologist are called upon for opinions and treatment. Likewise, the section on neoplastic diseases, while not covered exhaustively, brings into focus a field which is demanding increasing attention by all of those who see patients in this age group. The inclusion of some statistical data might have increased the usefulness of this work. A good bibliography of British and American references is included.

Although this book was written primarily for the pathologist, the pediatrician, the pediatric surgeon and pediatric resident will find this to be a valuable reference.

E. CLARENCE RICE

Systemic Lupus Erythematosus. A Mount Sinai Hospital Monograph, Edited by GEORGE BAEHR, M.D. AND PAUL KLEMPERER, M.D., 84 pages, illustrated, New York: Grune and Stratton, 1959, $3.75.

From the standpoint of the practicing pediatrician, the most significant section of this short monograph is the chapter, "Systemic Lupus Erythematosus in Childhood." In this paper Doctors Donald Gribetz and Walter L. Henley summarize previous information and thought on pathogenesis, symptomatology, treatment, and prognosis of this disease, and compare it to the experience at Mount Sinai over an 11 year period. The pattern of the disease is shown to be quite similar in all age groups, but in view of the low incidence in children (only 15 cases in 11 years at an active teaching center), its importance lies in its protean manifestations which may cause confusion in diagnosis. Among the diagnoses considered in the Mount Sinai patients were glomerulonephritis, leukemia, infectious mononucleosis, rheumatic fever, various arthritides, and allergic rash. Confirmation of the diagnosis, of course, depends on demonstration of the L.E. cell.

This is an interesting reference work, but because of its repetitive detail regarding pathology, hematology, and pathogenesis, it hardly needs a place in the library of the average pediatrician.

GEORGE J. COHEN, M.D.

The Care of Minor Hand Injuries. By ADRIAN EDE FLATT, M.A., M.D., F.R.C.S., 266 pages, 109 illustrations, St. Louis: The C. V. Mosby Company, 1959, $9.50.

This first edition of a very practical review of hand injuries has 266 pages with excellent explanatory diagrams. The text is divided into two parts. The first deals with a review of functional anatomy, principles of care, surgical techniques, and the classification and examination of injuries. It is recommended equally for medical students, internes, and surgical residents, both because it is so easy to read and understand, and also because the care it advises for hand injuries applies to the care of *any* wound commonly seen in the emergency room and private practice. The importance of the evaluation of hand injuries when first seen is impressed indelibly on the reader.

Part two deals with specific injuries or infections of the fingers and hands. Accurate diagnosis and treatment are clearly and simply defined. The problems of skin loss and treatment in vital areas are especially discussed from the point of view of both the conservative and the radical surgical requirements; the "do's and don'ts" in treatment are stressed in each chapter.

The surgically accepted tenets of this book show the crystallized opinions of an author with considerable experience. The medical student, interne, and surgical resident particularly will welcome the succinctness and clarity; there is little discussion of the opinions of others—yet an adequate bibliography is present for further reference. The general practitioner will find the evaluation and treatment of minor hand injuries presented in an easy-to-read fashion. The general surgeon who sees finger and hand injuries only occasionally will find the specific chapters as a quick reference for review. This book is a welcome addition to all libraries.

JOHN H. BAYLY, M.D.

CHILDREN'S HOSPITAL WASHINGTON 9, D. C.

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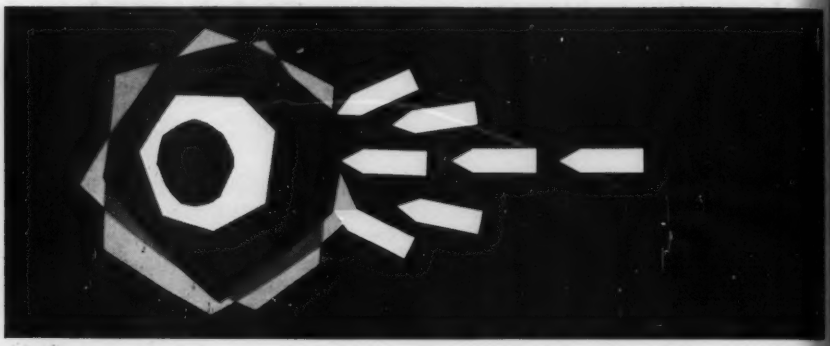

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